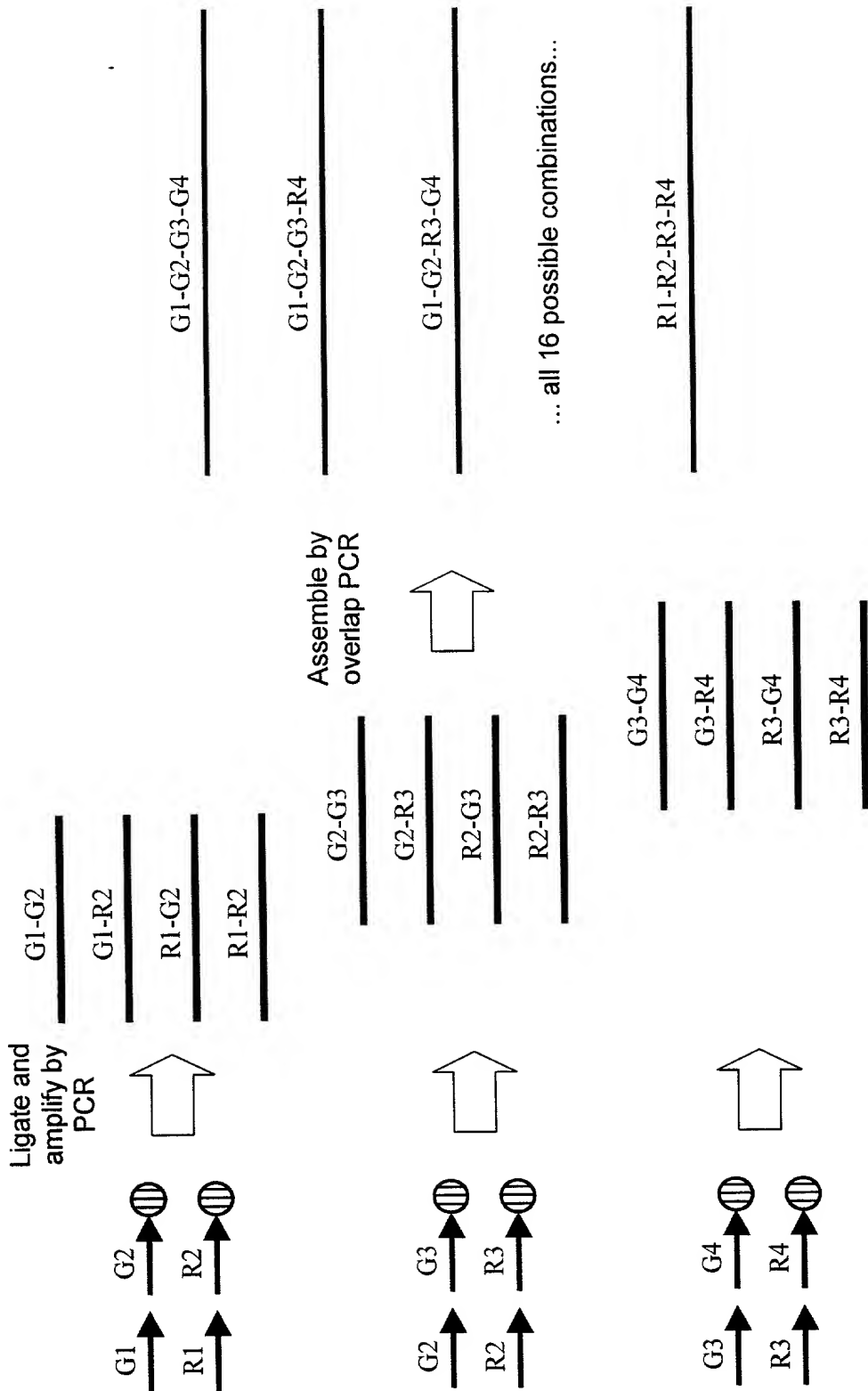
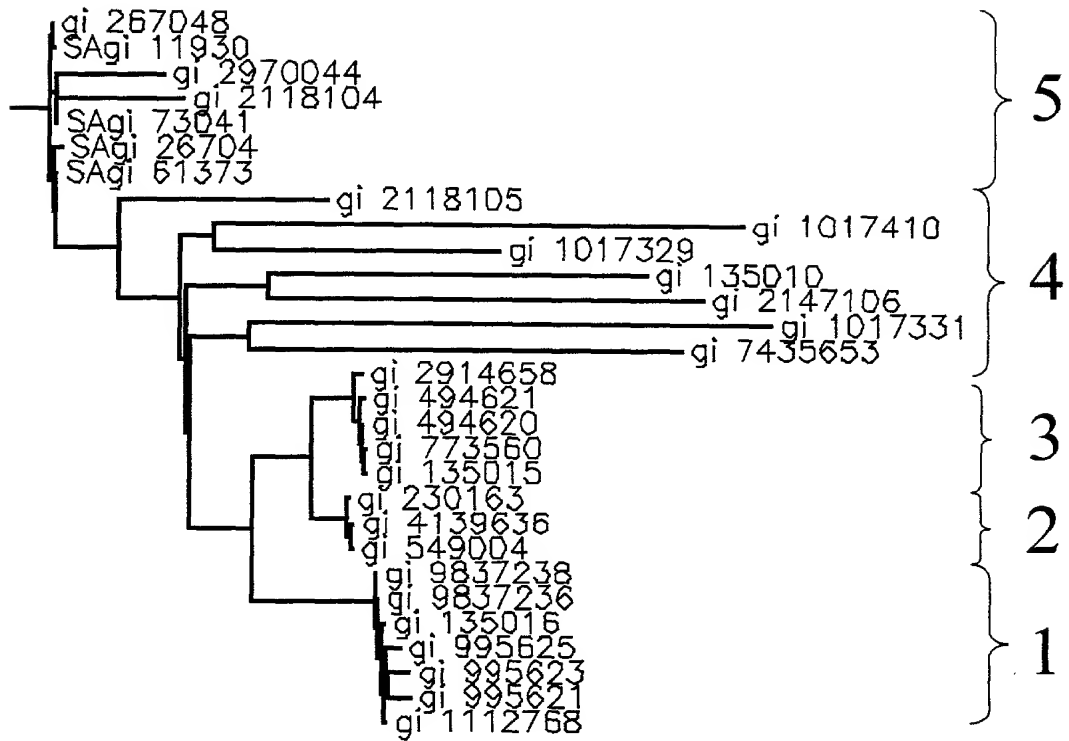


**Figure 1**



**Figure 2**



**Figure 3**

### Figure 4A

## Amino Acid Sequence Alignments for 29 Subtilisin Carlsberg Related Proteins

SAgi 11930	-----M	KKPLGKIVAS	TALLISVAFS	SS-----	-----
gi 267048	-----	-----	-----	-----	-----
SAgi 73041	-----	-----	-----	-----	-----
SAgi 61373	-----	-----	-----	-----	-----
SAgi 26704	-----	-----	-----	-----	-----
gi 2970044	-----M	NKKMGKIVAG	TALIISVAFS	SS-----	-----
gi 2118104	-----M	KKLFTKVVAS	AALLLSISLT	AT-----	-----
gi 2118105	MNLQKIRSAL	KVKQSALVSS	LTILFLIMLV	G-----	-----
gi 1112768	-----MMRK	KSFWLGMLTA	FMLVFTMAFS	DS-----	-----
gi 135016	-----MMRK	KSFWLGMLTA	FMLVFTMAFS	DS-----	-----
gi 9837236	-----MMRK	KSFWLGMLTA	LMLVFTMAFS	DS-----	-----
gi 995621	-----MMRK	KSFWLGMLTA	FMLVFTMAFS	DS-----	-----
gi 995623	-----MMRK	KSFWLGMLTA	LMLVFTMAFS	DS-----	-----
gi 995625	-----MMRK	KSFWFGMLTA	FMLVFTMEFS	DS-----	-----
gi 9837238	-----	-----	-----	-----	-----
gi 549004	-----MRS	KKLWISLLFA	LTLIFTMAF-	SN-----	-----
gi 4139636	-----	-----	-----	-----	-----
gi 230163	-----	-----	-----	-----	-----
gi 135015	-----MRG	KKVWISLLFA	LALIFTMAFG	ST-----	-----
gi 773560	-----	---MISLLFA	LALIFTMAFG	ST-----	-----
gi 494620	-----	-----	-----	-----	-----
gi 494621	-----	-----	-----	-----	-----
gi 2914658	-----	-----	-----	-----	-----
gi 1017329	-----	MKRRVHVLIM	TILMIVLATG	TA-----	-----
gi 2147106	---MKKFKR	KGRLLDEKHE	MAIFFLFLLV	IL-----	-----
gi 135010	-----M	KNMSCKLVVS	VTLFFSFLTI	GP-----	-----
gi 7435653	---MVAVVTG	VIQVGTKIAA	IAIALIFILP	LF-----	-----
gi 1017410	-----MKT	MKTLVIVIGV	LALLFIVAIG	HVRDQDQALI	QTKEIPKTLE
gi 1017331	-----MNKR	LKRWSAIMSI	VLLVNLLVPV	GT-----	-----

[illegible]

[illegible]

## Figure 4C

LIGFNS--D-	-----	KAKGLIQNAG	G-----	-----
IVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
IVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
IVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
IVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
IVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
FVGFKS--G-	-----V	KTAS--VKKD	IIKESGG--	-----
-----	-----	-----	-----	-----
IVGFKQ--T-	-----M	SAMSSAKKKD	VIKESGG--	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
IVGFKQ--T-	-----M	STMSAAKKKD	VIKESGG--	-----
IVGFKQ--T-	-----M	STMSAAKKKD	VIKESGG--	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
LVGFKN--E-	-----A	AVQAFSNNVT	TS-----	-----
MILFRH----	-----H	IDDGILKKYD	I-----	-----
IVVYKN----	-----K	AGKETILDSD	A-----	-----
VVIKINPE----	-----E	FNPKAVEALQ	G-----	-----
MLIGESTDDG	RLIGELNLE	FVKKYVKDIA	AVADTNGNFF	IGGDNPDVSW
IVTYKD----	-----V	VSESPDSRLS	VY-----	-----
-----	-----	-----	-----	-----
EEEEVEIELLH	EFETIPVLSV	ELSPED----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
VEDVEIDLH	EFDFIPVLSV	ELDPQD----	-----	-----
DESIEMELLY	EFEDIPVVS	ELSPED----	-----	-----
-----EIH	EYTEFFVIYA	ELPEAA----	-----	-----
-----KVDK	QFRIINAACA	KLDKEA----	-----	-----
-----KVDK	QFRIINAACA	KLDKEA----	-----	-----
-----KVDK	QFRIINAACA	KLDKEA----	-----	-----
-----KVDK	QFRIINAACA	KLDKEA----	-----	-----
-----KVDK	QFRIINAGKA	KLDKEA----	-----	-----
-----KVDK	QFRIINAACA	TLDKEA----	-----	-----
-----	--RIINAACA	KLDKEA----	-----	-----
-----KVQK	QFKYVNAAAA	TLDEKA----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
-----KVQK	QFKYVDAASA	TLNEKA----	-----	-----
-----KVQK	QFKYVDAASA	TLNEKA----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
-----AVEVQH	EYENLPVIVS	ELSTEV----	-----	-----
-----HAQK	KYETIPTVLA	ELNKSQ----	-----	-----
-----DVEQ	QYKHLPAVAV	TADQET----	-----	-----
-----KVIY	VADLAPVAII	SIPGKA----	-----	-----
QDQDERATQL	TSETVPGLGW	DIHVQSEGQE	EEGPAYHEHQ	AVIRFKPNRD
-----ENEQ	TMKTLPIKTM	TVPVSE----	-----	-----

FIG. 4C

**Figure 4D**

-----V	DALELDPAIS	YIE--EDA EV	TTM-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----V	EALDPAIS	YIE--EDA EV	TT-----	-----M QTV
-----V	KDLEKDPSIT	YIE--EDIEV	TIT-----	-----N QVT
-----V	SGLKNNPHID	FIE--ENEEV	EI-----	-----A QTV
-----L	KEVKNDPDVA	YVE--EDHVA	HAL-----	-----A QTV
-----L	KEVKNDPDVA	YVE--EDHVA	HAL-----	-----A QTV
-----L	EEVKNDPDVA	YVE--EDHVA	HAL-----	-----A QTV
-----L	KEVKNDPDVA	YVE--EDHVG	HGL-----	-----G QTV
-----L	KEVKNDPDVA	YVE--EDHVA	HVL-----	-----G QTV
-----L	KEVKNDPDVA	YVE--EDHVA	HAL-----	-----G QTV
-----L	EEVKNDPDVA	YVE--EDHVA	HAL-----	-----A QTV
-----V	KELKKDPSVA	YVE--EDHIA	HEY-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----V	KELKKDPSVA	YVE--EDHVA	HAY-----	-----A QSV
-----V	KELKKDPSVA	YVE--EDHVA	HAY-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----	-----	-----	-----	-----A QSV
-----A	QLENDPSVE	FIE--KNERV	YL-----	-----D PLV
-----V	DKLRSEPEIA	KVQANKTYKV	QS-----	-----Q IE
-----V	KELKQDPDIL	YVENNVSFTA	ADSTDFKVLS	DGTDTS DNFE
-----V	GLLSKLPGVV	SVSE DGVVQA	MAKPPWAGGG	NKS-QPAEVL
PAAWFATNPY	RVVEEAPFF	VIESPNQTTV	EIVEALSR--	DYDLDFAEPN
-----V	ERLKEDPNVV	SVSLDQPLQL	MSDTR-----	-----ELGEH
PWGISRVOAP	AAHNRGLT--	-----	-----GS	G---VKVAVL
PWGISRVOAP	AAHNRGLT--	-----	-----GS	G---VKVAVL
PWGISRVOAP	AAHNRGLT--	-----	-----GS	G---VKVAVL
PWGISRVOAP	AAHNRGLT--	-----	-----GS	G---VKVAVL
PWGISRVOAP	AAHNRGLT--	-----	-----GS	G---VKVAVL
PWGINRVQAP	IAQSRGFT--	-----	-----GT	G---VRVAVL
PWGITRVQAP	TAWTRGYT--	-----	-----GT	G---VRVAVL
PWGIPYIYSD	VVHRQGYF--	-----	-----GN	G---VKVAVL
PYGIPLIKAD	KVQAQGFK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGFK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGYK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGFK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGFK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGFK--	-----	-----GA	N---VKVAVL
PYGIPLIKAD	KVQAQGYK--	-----	-----GA	N---VKVAVL
PYGISQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI
PYGISQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI
PYGISQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI
PYGVSQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI
PYGVSQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI
PYGVSQIKAP	ALHSQGYT--	-----	-----GS	N---VKVAVI

FILED: 03-04-01

## Figure 4E

PYGVSQIKAP ALHSQGYT-- -----GS N---VKVAVI  
PYGVSQIKAP ALHSQGYC-- -----GS N---VKVAVI  
MNNIQETDIP KLEERMKR-- -----GD G---VKIAVL  
TWGYKKIYED SQYRSPFT-- -----GK G---VKVAVI  
QWNLEPIQVK QAWKAGLT-- -----GK N---IKIAVI  
PWGVDYIDAE LVWPDGVTGW VDV-----NGD GDGEIEVAVI  
YRFTKQIQAP VTPNDEFFKE YQWNLQQIDI EEGWSLASGE N---VKIAIL  
DWNNDMVKAF DAWDDGYT-- -----GK G---VKVAVF

DTGIST-HPD LN--IRGGAS FVPGEP-STQ -DGNGHGTHV AGTIAALNNS  
DTGIST-HPD LN--IRGGAS FVPGEP-STQ -DGNGHGTHV AGTIAALNNS  
DTGIST-HPD LN--IRGGAS FVPGEP-STQ -DGNGHGTHV AGTIAALNNS  
DTGIST-HPD LN--IRGGAS FVPGEP-STQ -DGNGHGTHV AGTIAALNNS  
DTGIST-HPD LN--IRGGAS FVPGEP-STQ -DGNGHGTHV AGTIAALNNS  
DTGISN-HAD LR--IRGGAS FVPGEP-NIS -DGNGHGTHV AGTIAALNNS  
DTGIST-HPD LN--IRGGVS FVPGEP-SYQ -DGNGHGTHV AGTIAALNNS  
DTGVAP-HPD LH--IRGGVS FISTEN-TYV -DYNHGTHV AGTVAALNNS  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DTGIQASHPD LN--VVGGAS FVAGEA-YNT -DGNGHGTHV AGTVAALDNT  
DSGIDSSHPD LN--VRGGAS FVPSET-NPY QDGSSHGTHV AGTIAALNNS  
DSGIDSSHPD LN--VRGGAS FVPSET-NPY QDGSSHGTHV AGTIAALNNS  
DSGIDSSHPD LN--VRGGAS FVPSET-NPY QDGSSHGTHV AGTIAALNNS  
DSGIDSSHPD LK--VAGGAS MVPSET-NPF QDNNSHGTHV AGTVAALNNS  
DSGIDSSHPD LK--VAGGAS MVPSET-NPF QDNNSHGTHV AGTVAALNNS  
DSGIDSSHPD LK--VAGGAS MVPSET-NPF QDNNSHGTHV AGTVAALNNS  
DSGIDSSHPD LK--VAGGAS MVPSET-NPF QDNNSHGTHV AGTVAALNNS  
DSGIDSSHPD LK--VAGGAS FVPSET-NPF QDNNSHGTHV AGTVAALNNS  
DTGIAS-HDD LH--VIDGVS FVSVEP-FYR -DLNGHGTHV AGTIAAQEND  
DTGIASNHPD LK--VKGGTC VIRSDCGKGY NDDNGHGTHV AGIIGALDNG  
DSGISP-HDD LS--IAGGYS AVSYTS--SY KDDNGHGTHV AGIIGAKHNG  
DTGVDKDHPD LAGNIVWGIS VLNGRISSNY QDRNGHGTHV TGTVAALDND  
DTGVDPNHPD IKDKIVNGYN AVEGNN--NF ADKHGHGTHV AGVAAAVTNN  
DTGFDG-HQD IT--YAGGHS VFEGEP--YT HDHHGHGTHV AGIIGAREGT

I-GVLGVAPN AELYAVKVLG ASGSGSVSSI AQGLEWAGNN G-----MH--  
I-GVLGVAPS AELYAVKVLG ASGSGSVSSI AQGLEWAGNN G-----MH--  
I-GVLGVAPS AELYAVKVLG ASGSGSVSSI AQGLEWAGNN G-----MH--  
I-GVLGVAPS AELYAVKVLG ASGSGAISSI AQGLEWAGNN G-----MH--  
I-GVLGVAPS AELYAVKVLG ADGRGAISSI AQGLEWAGNN G-----MH--  
I-GVLGVAPN VDLYGVKVLG ASGSGSISGI AQGLQWAANN G-----MH--  
I-GVVGVPAPN AELYAVKVLG ANGSGSVSSI AQGLQWTAQN N-----IH--  
Y-GVLGVAPG AELYAVKVLD RNSGSGHASI AQGIEWAMNN G-----MD--  
T-GVLGVAPS VSLYAVKVLN SSGSGSYSGI VSGIEWATTN G-----MD--  
T-GVLGVAPS VSLYAVKVLN SSGSGTYSGI VSGIEWATTN G-----MD--  
T-GVLGVAPN VSLYAVKVLN SSGSGSYSGI VSGIEWATTN G-----MD--  
T-GVLGVAPS VSLYAVKVLN SSGSGSYSGI VSGIEWATTN G-----MD--  
T-GVLGVAPS VSLYAVKVLN SSGSGSYSI VSGIEWATTT G-----MD--

101200-001-000



[illegible]

## Figure 4G

--AG---NVG	FPARYANAMA	VGATDQNNNR	ASFSQYGAGL	DIVAPGVGVQ
--SG---TVS	YPARYANALA	VGATDQNNNR	ASFSQYGTGL	NIVAPGVGIQ
QGGGS--NNMG	YPARYASVMA	VGAVDQNGNR	ANFSSYGSEL	EIMAPGVNIN
S-SGNTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGNTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGNTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGNTNTIG	YPAKCDVIP	VGGEDSNSNR	SSFSSVGAEI	EVMAPVSGVY
S-SGNTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGYTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGNTNTIG	YPAKYDSVIA	VGAVDSNSNR	ASFSSVGAEI	EVMAPGAGVY
S-SGSTSTVG	YPAKYPSTIA	VGAVNSSNQR	ASFSSVGSEL	DVMAPGVSIQ
S-SGSTSTVG	YPAKYPSTIA	VGAVNSSNQR	ASFSSAGSEL	DVMAPGVSIQ
S-SGSTSTVG	YPAKYPSTIA	VGAVNSANQR	ASFSSAGSEL	DVMAPGVSIQ
T-SGSSSTVG	YPGKYPSVIA	VGAVDSSNQR	ASFSSVGPEL	DVMAPGVSIQ
T-SGSSSTVG	YPGKYPSVIA	VGAVDSSNQR	ASFSSVGPEL	DVMAPGVSIQ
T-SGSSSTVG	YPGKYPSVIA	VGAVDSSNQR	ASFSSVGPEL	DVMAPGVSIQ
T-SGSSSTVG	YPGKYPSVIA	VGAVDSSNQR	ASFSSVGPEL	DVMAPGVSIQ
T-SGSSSTVG	YPAKYPSVIA	VGAVDSSNQR	ASFSSVGPEL	DVMAPGVSIQ
E-ADKQHTID	YPARYDSVVA	VGAVDGNNER	ASFSSYGEQL	EIMAPGVEIH
S-VGSKNTIL	YPAKYSSVIA	VGSVDSRLQR	LPFSATGPPEL	EIVAPGQYVF
---GNGKPVN	YPAAYSSVVA	VSATNEKNQL	ASFSTTGDEV	EFSAPGTNIT
----GADSPS	YPAAYPEVIA	VGAIENGNV	PSWSNRNPE-	-VAAPGVNIL
-----VEDPL	YPAIYEEVLT	VAAVDDTRNR	AFFSNFGKHI	DVTAPGEHIP
KADGSGETIE	YPAKYDEVIA	VASVDKEMKR	TNTSATGVEN	ELAAPGHLIG
STYPGSTYAS	-----L	NGTSMATPHV	AGAAALVKQK	-----NP
STYPGSTYAS	-----L	NGTSMATPHV	AGAAALVKQK	-----NP
STYPGSTYAS	-----L	NGTSMATPHV	AGVAALVKQK	-----NP
STYPGSTYAS	-----L	NGTXMATPHV	AGAAALVKQK	-----NP
STYPGSTYAS	-----L	NGTSMATPHV	AGAAALVKQK	-----NP
STVPNGYSS	-----F	NGTSMATPHV	AGVAALVKQK	-----NP
STYPGNRYAS	-----L	SGTSMATPHV	AGVAALVKQK	-----NP
STYLNNGYRS	-----L	NGTSMASPHV	AGVAALVKQK	-----HP
STYPTNTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STYPTSTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STYPTSTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STYPTNTYTT	-----L	NGTSMASPHV	AGTSALILSK	-----HP
STYPTNTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STYPTNTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STYPTSTYAT	-----L	NGTSMASPHV	AGAAALILSK	-----HP
STLPGGTYGA	-----Y	NGTSMATPHV	AGAAALILSK	-----HP
STLPGGTYGA	-----Y	NGTCMATPHV	AGAAALILSK	-----HP
STLPGGTYGA	-----Y	NGTSMATPHV	AGAAALILSK	-----HP
STLPGNKYGA	-----Y	NGTSMASPHV	AGAAALILSK	-----HP
STLPGNKYGA	-----Y	NGTSMASPHV	AGAAALILSK	-----HP
STLPGNKYGA	-----Y	SGTCMASPHV	AGAAALILSK	-----HP
STLPGNKYGA	-----K	SGTCMASPHV	AGAAALILSK	-----HP
STLPGNKYGA	-----K	SGTSMASPHV	AGAAALILSK	-----HP
STFLFNRYER	-----L	SGTSMASPHV	TGAAALIKSN	-----NP
STFPINLDTT	DGKKDGYTAL	SGTSMALPHL	YTGALAATLK	-----TS
STYLNQYYAT	-G-----	SGTSQATPHA	AAMFALLKQR	-----DP
STYPDDTYEE	-----L	SGTSMATPHV	SGTVALIQAA	RLAAGLPLLP

401220-307E-600

### Figure 4H

[illegible]

### Figure 4I

```

-----VQAAAQ-----
-----VQAAAQ-----
-----VQAAAQ-----
-----VQAAAQ-----
-----VDAALD-----
--TLSSDMAV KAVK----- ADNGLWS--- ---SRS-ISP IPFK--SLAE
--DSAYAAAE QAVK----- KAEQTKAQID INKARELISQ LPNSDAKTAL
---AYDAVQ TAVS----- S-----
---IEAALK AIRT----- S-----
EESPAENPOE QPSDGKENEG SEDQGSTPPD EEENEESPAE DPQEQPSDGK

```

KKRRNGGRHY	KQ-----	-----	-----	-----
HKRLDKVQSY	RNVKDAKDKV	AKAEKYKTQQ	T-----	-----VDTA
ENKGSENOGS	TPPDEEENE	SPEVPQEOP	SDGKENEGSE	DQGSTPPDEE

[illegible]

### Figure 4J

QTAINKLPNG	TDKKNLQKRL	DQVKRYIASK	QAKDKVAKAE	KSKKKTDVDVS
-----	-----	-----	-----	-----
ENEESPAEDP	QEQPSDGKEN	EESKNPDSAP	PAGEKEGKQT	ARVQVKPVNL
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
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-----	-----	-----	-----	-----
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-----	-----	-----	-----	-----
-----	-----	-----	-----	-----
AQSAIGKLPA	SSEKTSLQKR	LNVKSTNLK	TAQQSVSAAE	KKSTDAN---
-----	-----	-----	-----	-----
GGVAIVSNAD	VASVLDNRTL	VVFFDSALDD	LTRLALTADQ	VKELKDRGIT

[illegible]

### Figure 4K

[illegible][illegible]

### Figure 4L

KDKTALOKRL DKVKKKVAAB EAKKVETAKA KVKKAEKDKT KKS KTS AQSA

ONGOOVRHFD EEIEMGFRVD QEKNVNNLKI YYWNESLNEW EKIGGNYQEG

VNQLKASNEK TKLQKRLNAV KPKK-----

FIVARTNHFS TYTVFDSAVF EETKSGTPIS GGKTNGNSTT EGTTRNGTSK

### Figure 4M

NGTGSEPQAE ESNEQNNKDG TLPKTATNLY NSLAIGALLL LIGFVLLRKS

-----

KRRIVE